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**RESPONSE TO EPA COMMENTS ON THE
FND CATIONICS CATEGORY HPV SUBMISSION
September 4, 2003**

GENERAL COMMENTS

One of the most important components of the FND Cationics Test Plan is the use of the studies for the Phase III/IV Pesticide Reregistration under FIFRA for didecyldimethylammonium chloride (DDAC; CAS RN 7173-51-5) and alkyldimethylbenzyl ammonium chloride (ADBAC CAS RN 68424-85-1). The FND Cationics Task Group (Task Group) believes that both of these chemicals are appropriate for inclusion in the Cationics Category, consistent with the EPA's own assessment of the quaternary amine biocides [see Assessment of Data Availability – p. 2].

These studies are available to EPA in the Pesticide Registration Program and many of the studies for ADBAC have formally issued Data Evaluation Reports (DER) as included in the original submission (Appendix B). DDAC studies have been submitted to the EPA for the Pesticide Reregistration Program and a summary of the studies with MRID Submission numbers that are pertinent to the High Production Volume (HPV) Chemical Challenge Program are summarized in Table 1 (attached).

Due to efforts of the registrants to preserve data confidentiality, Robust Summaries for DDAC and ADBAC cannot be provided for the HPV Program [see Assessment of Data Availability – p. 1]. However, as described in the original submission, EPA and other government reviews of these studies adequately support their use for the HPV requirements.

All of these ADBAC and DDAC studies are reliable and were submitted and are available to EPA in order to obtain registration under FIFRA. Therefore, the Task Group considers it appropriate to use these studies a priori for the HPV Chemical Challenge Program.

The Task Group also believes that a second key factor in the evaluation of the data for the FND Category Chemicals is the behavior of these and similar chemicals in the environment. As delineated in the Assessment of Data Availability (p. 15 and others), cationic substances in the environment instantaneously form complexes with naturally occurring negatively charged constituents in sewage, soils, sediments and with dissolved humic substances in surface waters. This complexation behavior results in reduced bioavailability under actual environmental conditions not adequately represented by standard laboratory assays and/or predictions by EPIWIN SAR models. Thus the extreme variability of the measured values is predictable and has been reported in the literature and Pesticide Registration documents.

RESPONSE TO SPECIFIC EPA REQUESTS/COMMENTS

In the discussion below, the EPA's comments are directly quoted in bold, italic font followed by the FND Cationic Task Group's response.

1) The submitter, however, needs to provide full robust summaries for DDAC.

As noted above, due to confidentiality issues, the Task Group has been unable to obtain the full study report from the registrants. Hence, the Task Group isunable to create or provide Robust Summaries for DDAC. However, an extensive battery of studies – well beyond the requirements of the program – are already in EPA's possession (Table 1, attached). Furthermore, these studies have also been reviewed and accepted by the Canadian Government (original submission; Appendix B). The mere lack of Robust Summaries should therefore not exclude the use of these high quality studies in the

HPV Program because: 1) they are reliable; 2) summaries as provided in the original submission are available; and 3) rejection for lack of the specific Robust Summary format could lead to the unnecessary use of experimental animals for testing already completed. Furthermore, these studies will be reviewed and summarized in a Registration Eligibility Decision (RED). The RED will be publicly available after EPA has completed its review.

2) EPA believes that ADBAC should not be used as an analog for the human health endpoints because of structural differences from the category members. However, the use of ADBAC for ecological effects is acceptable and the submitter should provide the necessary robust summaries.

As previously described, a full dataset is available for both ADBAC and DDAC within the Pesticide Reregistration program. All endpoints, including those not required (e.g. avian studies, metabolism studies, cancer bioassays) in the HPV Chemical Challenge Program, show these molecules to have a very similar toxicologic profile. Further, the HPV reviewer's comment is inconsistent with EPA's own evaluation of the quaternary ammonium biocides and the results of the numerous studies for human health effects. Although official acceptability of the approach has not been published by the EPA, data for ADBAC have been submitted for similar quaternary amine biocides, with and without benzene substitution, and the Agency has accepted ADBAC data for this purpose. The EPA's acceptance of ADBAC data is based on the similarity of the specific effects and dose response for evaluation of potential environmental and human health hazards, as well as exposure, for ADBAC, DDAC, and other quaternary amines.

The Task Group does not agree that there are significant structural differences between ADBAC and DDAC, again consistent with the EPA's own determinations in the Pesticide Reregistration program. However, even if structural diversity were a concern, the similarity in toxicologic profile for ADBAC, DDAC and other quaternary amine chemicals with somewhat different structures provides reassurance for use of a category approach for the FND Cationic Category chemicals.

The Task Group agrees that the use of ADBAC for ecological endpoints is consistent and appropriate for evaluation of the FND Cationics Category and the difference in approach for environmental and human health-related evaluations in the HPV Chemical Challenge Program is unclear.

It is also important to recognize that refusal to accept ADBAC data in support of the potential human health effects of the FND Cationic Category chemicals could result in unnecessary costs and the unwarranted use of laboratory animals.

As noted above, The Task Group is unable to provide Robust Summaries for ADBAC but EPA's DERs were included in the original submission (Appendix B).

3) …the submitter needs to provide measured data, according to OECD guidelines, for the following chemicals: CAS # 61789-77-3, CAS # 68002-59-5, CAS # 61789-80-8, and CAS # 61789-81-9.

Due to the inherent variability of the fatty acid source, many of these chemicals are not discrete as described in the Assessment of Data Availability. Thus, these chemicals fall under the TSCA Class II (variable composition, i.e., the percentage of each alkyl group in the range can vary depending on the source) category of chemicals recognized by EPA as distinct from those chemicals with defined structures. Measurements such as melting point and boiling point are typically provided as ranges and therefore provide minimal information for these Class II chemicals since they do not identify key characteristics of the molecules. Further, these chemicals do not exist commercially as pure chemicals and are always in solution. Therefore, melting point and boiling point cannot be determined without manipulation to produce purified chemicals that do not exist in commerce. The effort required to produce these purified materials and conduct the measurements is not expected to further the understanding of the fate and effects for screening in the HPV Chemical Challenge Program

particularly in light of the more than adequate data to support the environmental and human health effects of these chemicals.

4) Water Solubility. The submitter provided measured data for 1 test mixture and estimated values for the 3 discrete compounds in this category. It is not possible to extrapolate the water solubility for the chemicals in this category based solely on the information provided by the submitter. The submitter needs to provide measured data, according to OECD guidelines, for the following chemicals: CAS # 8030-78-2, CAS # 67784-77-4, and CAS # 68607-29-4.

As documented in the Data Assessment document, complex issues related to chemical form (e.g. chloride salt), adsorption, physical form in the environment, toxicity related to physical properties (not chemical) etc. exist for this category of chemicals. Specific water solubility values are of no relevance to determination of environmental effects. Indeed, many surfactants are toxic to aquatic organisms due to physical properties when the surfactant is NOT soluble in water. Such effects must be determined and put into context with potential exposure and specific environments. This type of risk assessment is beyond the scope of the HPV Chemicals Challenge Program.

As noted above, the determination of specific water solubility does not further the understanding of the environmental fate and effects because these chemicals exist in solutions, not as pure chemical entities.

It should also be noted that DDAC and ADBAC, along with other quaternary amines registered as biocides are undergoing detailed risk assessments in the Pesticide Reregistration Program, the EU Biocidal Products Directive, and other programs. These efforts will provide a much more detailed and useful evaluation of the environmental fate and effects than can be gained by attempting to determine a specific water solubility under the HPV Chemicals Challenge Program.

5) Biodegradation. The submitter indicates in its test plan that "there are adequate measured data across the FND Cationics Category to allow the conclusion that these chemicals are biodegradable although tests are frequently confounded by adsorption phenomena." While there are adequate data for most of the chemicals in this category, EPA believes that the submitter's conclusion is misleading. The data provided by the submitter, in addition to data available from other sources, show that these chemicals have widely varying rates of biodegradation, indicating that some biodegrade rapidly and others don't. The submitter needs to revise its conclusions in order to reflect this more accurate description of the data. Furthermore, EPA believes that the structure of CAS No. 67784-77-4 is sufficiently different from other compounds in the category that the submitter needs to provide data for this chemical following OECD guidelines.

The Assessment of Data Availability (page 11-12) reviews the spectrum of biodegradation results and conclusions for specific test conditions. The Task Group does not agree that the conclusion is "misleading". The conclusion clearly states that the reported results are "confounded" by the environmental behavior of the FND Category chemicals. The adsorption of the FND Cationic Category chemicals to organic matrices poses significant study design problems when evaluating biodegradation. In addition, many of these chemicals have biocidal properties that can affect the results of standard laboratory tests from toxicity to the microorganisms. When properly evaluated in a risk assessment setting, these chemicals have been shown to biodegrade when bioavailable and at concentrations that are sublethal to the microorganisms. However, such detailed evaluations require careful consideration of the environmental conditions and exposure of the chemicals in the assay that are beyond the scope of a screening program. Therefore, additional, routine biodegradation studies, as

appropriate to the HPV Challenge Program, are not expected to further the understanding of the environmental fate of the FND Cationic Category Chemicals.

6) Transport and Distribution (fugacity). Results from a level III fugacity model are presented only in Table 3 of the test plan and details on the input parameters used to run the model are not provided. The submitter needs to provide these data in robust summary format and present the inputs used to run the model.

Robust Summaries (numbers 1- 5) for the fugacity models are included in the Supplement to Appendix A (attached). Please note that some values may have changed slightly from the original submission because of changes in the version of the model software.

7) Reproductive Toxicity. No reproductive toxicity studies were submitted for any of the category members. This endpoint is addressed by adequate histopathology of the reproductive organs in subchronic studies conducted on two category members and data from two developmental toxicity studies conducted on DDAC. However, EPA recommends also conducting a reproduction/developmental screening test (OECD Guideline 421) on CAS No. 68607-29-4 because there is no reproductive/developmental toxicity information for the monoalkyl category members.

As described in the Assessment of Data Availability (p. 15), the evaluation of reproductive organs in repeated dose studies for the two category chemicals along with the 2-generation reproduction studies for DDAC and ADBAC are adequate to support the conclusion that the FND Cationics Category chemicals are not reproductive toxins. It is unclear why the reviewer has not considered these two multigeneration studies while referencing developmental toxicity studies in this comment. The Task Group believes that the additional use of experimental animals to conduct a limited-scope reproductive screening study on one of the FND Cationic Category chemicals will not further the understanding of potential human health hazards to these chemicals. Detailed evaluations over multigenerations have not reported concern for reproductive effects.

8) Developmental Toxicity. The data for the category members were not adequate to address this endpoint; however, two studies on DDAC appear to provide adequate data and provide data for two different species. As stated above, EPA recommends that the submitter conduct a test using OECD Guideline 421 on CAS No. 68607-29-4 to adequately cover this endpoint for the monoalkyl category members.

The Task Group points to five Robust Summaries for developmental toxicity studies for the FND Cationics Category chemicals (CAS RN 112-00-5, 112-02-7, 112-03-8, 68783-78-8, and 61789-81-9) summarized in the Data Assessment document (p. 15). In addition, information on two developmental toxicity studies for DDAC and two for ADBAC were provided. Thus, for the 13 chemicals included in the FND Cationics Category, nine developmental toxicity studies were available. None of these studies showed significant developmental toxicity or teratogenicity thus supporting the conclusion that the FND Cationics Category chemicals are not developmental toxicants.

9) The submitter needs to provide additional algae toxicity data and a daphnid 21-day chronic toxicity study to complete a read-across approach for this category. EPA recommends providing these data for CAS No. 112-00-5 because this chemical has a short chain length (and is thus likely to be fairly water soluble). The chemical's water solubility plus the toxicity observed in 7-day fish and daphnid studies indicate that it is likely to be toxic in the recommended 21-day daphnid study (for the invertebrate chronic toxicity endpoint, EPA considers only the 21-day daphnia study (e.g., OECD guideline 202) acceptable for the purposes of the HPV Challenge Program.

The aquatic toxicity of the FND Cationics Category chemicals is similar in fish, daphnia and algae. In all observed cases, when the chemicals are bioavailable, the chemicals are toxic to aquatic species. Further, the effective concentrations at which toxicity is manifested are similar across chemicals and species. The adsorption characteristics of these chemicals mitigates their toxicity in real-world situations. The anticipated mechanism of toxicity, (physical rather than chemical) indicates that more detailed testing of these chemicals will not further the understanding of the toxicity. For example, the Robust Summary for fish toxicity in the original submission (Appendix A) shows that DTDMAC (CAS RN 68783-78-8) is made non-toxic at approximately a 5:1 ratio of suspended solids to chemical concentration while there was 80% mortality at a 2:1 ratio. Specific EC_{50} and LC_{50} values will be highly variable. General conclusions about the toxicity of the chemicals can be made using the current information. Although chronic toxicity studies are not a specific requirement under the HPV Chemical Challenge Program, there is a substantial body of information regarding chronic toxicity to aquatic organisms available [see Assessment of Data Availability pp. 12-13 and associated Table 3]. Chronic daphnia studies are available for one HPV and 2 supporting chemicals. Therefore, it is unclear why this comment indicates that "only a 21-day daphnia study… [is] acceptable". Further, these chronic studies support what is routinely observed in the acute studies, specifically that the chemicals are toxic to aquatic organisms when they are bioavailable. Therefore, the Task Group believes that additional testing, particularly using standard guidelines (e.g. OECD 202) will not further the understanding of the chronic toxicity of these chemicals in the environment.

10) In Table 3 of the test plan, the first entry of acute LC50 fish toxicity values for CAS No. 68783-78-8 should be "0.62 to 3.0 mg/L." The table states that the range is up to 24.0 mg/L; however, this upper limit involved a different aspect of the test in which suspended solids were added.

The comment is noted. The range in the table was intended to provide the total range for the available data. The range of 0.63 to 3.0 mg/L was for laboratory water. The higher values were from tests conducted using water from the Town River (10.1 to > 24 mg/L). This difference clearly shows the mitigation of toxicity when adsorption in the environment is possible.

11) The submitter needs to correctly identify the chemical associated with CAS No. 112-02-7 (see robust summary comments for CAS No. 112-00-5).

There is no error in the definition of hexadecyltrimethyl ammonium chloride (CAS RN 112-02-7) throughout the Data Assessment and Test Plan documents. See discussion below regarding an error in one Robust Summary.

CONCLUSIONS

The FND Cationics Task Group has carefully reviewed EPA's comments and addressed them in the above responses. In view of the extensive data availability, low order of mammalian toxicity, and the complexity of ecotoxicity and environmental fate studies, and with regard to the HPV Program's directives to avoid unnecessary use of experimental animals, the Task Group concludes that further testing of the chemicals in the FND Cationics Category is unwarranted and would not further the understanding of the hazards of these chemicals within the scope of the HPV Chemical Challenge Program.

ROBUST SUMMARY COMMENTS

1) For all endpoints, robust summaries should be prepared for the DDAC studies presented in Appendix B and assign reliability codes to these studies.

See previous comments above (page 1) on DDAC study availability. All DDAC studies included in the Assessment of Data Availability and Test Plan are Reliable (Klimisch Code = 1A) and are used for the FIFRA registration of DDAC (Table 1, herein).

2) Acute Toxicity. The submitter needs to add the following information to summaries where the data are missing: age and weight of the test animals, length of the acclimation period, housing and feeding conditions, purity of the test compound, and/or analytical methods used.

Where available, the additional information for each study is included in the attached revised Robust Summaries. In some cases, when studies were conducted prior to GLP regulations and guideline development, or when studies were conducted for product stewardship purposes without formal regulatory compliance, details of the studies are not available. However, such studies still represent a broad body of knowledge of industrial products and support the overall conclusions of the evaluations for the HPV Cationics Category. Appropriate Reliability scores are provided for each situation.

3) Repeated-Dose Toxicity. Robust summaries were submitted for three dermal studies and three oral studies. Because the submitter did not identify key studies for this category, EPA identified (and evaluated) three oral studies as key studies (one for a category member, CAS No. 61789-81-9, and two for non-category members DDAC and TMAC. The robust summary for TMAC provided adequate data. However, the submitter needs to provide a robust summary for DDAC and the purity of the test substance for CAS No. 61789-81-9.

See previous comments on DDAC study availability and general availability of specific data.

4) Genetic Toxicity - Gene Mutations. Data from an Ames test using CAS No. 112-03-8 were judged to be inadequate because only two S. typhimurium strains were used and the concentrations tested were not specified. Data from two Ames tests with CAS No. 112-02-7 were judged inadequate because only two strains were tested and in one of the two tests, concentrations were not provided. The results of all tests were negative with one exception. Positive results were seen in an Ames test using CAS No. 8030-78-2 in one of five S. typhimurium strains (TA1538) with and without metabolic activation.

The Assessment of Data Availability (p. 15) acknowledges the limitations of the bacterial mutation studies with only two strains. The Task Group does not agree, however, that these studies are "inadequate" in that they provide information on the lack of effects in at least two strains of bacteria. This information supports the more reliable and robust evaluations for a body of mutagenicity assays for a substantial number of chemicals in the FND Cationic Category as well as DDAC, TMAC and ADBAC [see Assessment of Data Availability, p. 15 and associated Table 4]. The Task Group restates its view that the available data indicate that these chemicals are unlikely to be mutagenic. Overall, the Task Group believes that the available data are adequate for the HPV Chemical Challenge Program.

5) Genetic Toxicity - Chromosomal Aberrations. Data from an in vivo rat bone marrow chromosomal aberration test with TMAC were judged inadequate because the cells were harvested too soon after treatment (8 and 12 hours).

Some studies used in the Test Plan development, such as this assay, do not meet all current guideline requirements. The Task Group believes that these studies add to the weight of evidence for evaluation of the category chemicals and should not be excluded from the overall data assessment.

6) Reproductive Toxicity. In addition to providing robust summaries for appropriate studies for DDAC from Appendix B and assigning a reliability rating to this study, EPA also recommends that the submitter include robust summaries that report results of the reproductive organ evaluation from the available repeated-dose studies.

The repeated-dose studies for which reproductive organ evaluations were made are included in the section on Repeated Dose studies. The Robust Summaries state that "Reproductive organs weighed and examined microscopically adequate for SIDS reproductive screening". The Robust Summaries were not recopied for the Reproductive endpoint but would be identical.

7) The robust summaries need to be expanded to include additional information. Where appropriate, the submitter needs to provide information on the amount of suspended solids used in the test system because the addition of suspended solids can substantially change the toxicity of the FNDs. Also, the summaries need to discuss whether the purity of the chemicals was taken into consideration when determining the LC50s. In some cases, the purity of the test chemical was as low as 35 percent. Finally, in several cases, the submitter needs to add methodological details (e.g., DO, pH, water hardness) if available. Selected chemical-specific comments are discussed below.

The attached revised Robust Summaries address this comment when the information is available. However, unavailability of specific information does not preclude the use of some studies because they provide weight of evidence for understanding the fate and effects of the FND Cationics Category chemicals.

RESPONSE TO SPECIFIC ROBUST SUMMARY COMMENTS

CAS No.112-00-5

Fish. The second robust summary in Section 4.1 reports the chemical as dodecyltrimethylammonium chloride but the CAS No. as 112-02-7 (which is the number for hexadecyltrimethylammonium chloride). In addition, the size and length of the fish at test initiation are identical in the first and second summaries. The submitter should clarify these issues. If the results are for the same chemical from the same test, the submitter should consider possible reasons that the 24-hr LC50 value is lower than the 96-hr value. Missing data elements include pH, water temperature, water hardness, total organic carbon (TOC), dissolved oxygen (DO) content, and whether results are corrected for test substance purity.

The second robust summary has the incorrect chemical name but the correct CAS RN (i.e. this summary is for hexadecyltrimethylammonium chloride; CAS RN 112-02-7). A corrected Robust Summary is attached (Robust Summary #6). The Task Group's reporting of the data is accurate. The first three Robust Summaries for this endpoint come from the same study. In this study, the range of length and body weight was specified for the entire population used in the study, not for each chemical. Therefore, the specified range is the same for all three chemicals. Further, the study tested

the same concentration of a number of chemicals and, when significant toxicity was observed at 24 hours, only the 24-hour LC_{50} was reported (i.e. no fish were available to determine an LC_{50} for a longer time period).

The test chemical purity of 50% is in water and the concentrations are as active ingredient. Thus, the stated LC_{50} is correct for this chemical.

Some studies used in the Test Plan development, such as this assay, do not meet all current guideline requirements. The Task Group believes that these studies add to the weight of evidence for evaluation of the category chemicals and should not be excluded from the overall data assessment.

Invertebrates. Missing information includes water temperature, TOC, and percent active ingredient used to determine the results.

A revised Robust Summary (#13) is provided in the Supplement to Appendix A, attached. Water temperature and TOC are not provided in the report. Some studies used in the Test Plan development, such as this assay, do not meet all current guideline requirements. The Task Group believes that these studies add to the weight of evidence for evaluation of the category chemicals and should not be excluded from the overall data assessment.

The test material was 35% active ingredient in water. Therefore, it is logical to assume that the "nominal concentrations" from which the LC_{50} value was determined are active ingredient. Thus, no correction should be made and 0.39 mg/L is the appropriate LC_{50} value for this chemical. In support of this conclusion, the LC_{50} value is consistent with that of other chemicals in the FND Cationics Category.

CAS No. 112-02-7

Fish. Data are invalid because only a 24-hour test was submitted rather than the accepted 96-hour test.

As noted above (Robust Summary #6), the method of testing yielded only a 24-hour value based on toxicity. The data are valid but the study does not meet all current guideline requirements. The Task Group believes that the study adds weight of evidence for the evaluation of this chemical and other Category chemicals and should not be excluded from the overall data assessment.

CAS No. 8030-78-2

Invertebrates (acute). All three tests should have separate robust summaries containing the following missing data: pH, DO, water temperature, TOC, and result values corrected for 100 percent active ingredient.

A Robust Summary for each water type (Robust Summaries 14-16) is included in the Supplement to Appendix A, attached.

The report does not provide information other than hardness for the water sources used in the acute toxicity studies. More data were presented for the chronic toxicity studies as included in the revised Robust Summary (see below).

The determination of chemical concentration in the studies was by radiolabel. Therefore, the concentrations must be as active ingredient and LC_{50} values reported are appropriate for this chemical.

Invertebrate reproduction (21-day daphnid). Missing data elements include: DO, TOC, pH, water temperature for both river and well water experiments, LOEC value, and results corrected for 100 percent active ingredient.

Data (except TOC, which is not reported) have been added to each Robust Summary (# 22 and 23) included in the Supplement to Appendix A, attached. See comment above related to % active ingredient.

CAS No. 112-03-8

Fish. Missing data elements are pH, water temperature, alkalinity, DO, TOC, number of fish per number of replicates, water hardness, and test value corrected for 100 percent active ingredient.

The test chemical purity of 50% is in water and the concentrations are as active ingredient. Thus, the stated LC_{50} is correct for this chemical.

Some studies used in the Test Plan development, such as this assay, do not meet all current guideline requirements. The Task Group believes that these studies add to the weight of evidence for evaluation of the category chemicals and should not be excluded from the overall data assessment.

CAS No. 68783-78-8

Fish. For both tests using Lepomis machrochirus, missing data include TOC, DO, and the 95% confidence limit. The third test using Cyprinidon variagatus is missing water hardness, pH at the time of test, TOC, and DO. Also, the 96-hr LC50 is listed as 24.0 mg/L; however, the 95% confidence interval is stated as "9.5 – 6.3 mg/l." The submitter should correct this apparent error.

Confidence intervals have been added or revised where appropriate in the Robust Summaries (# 11 and 12). TOC and DO were not reported for L. machrochirus. The requested information for C. variegatus was not reported.

Some studies used in the Test Plan development, such as this assay, do not meet all current guideline requirements. These studies add to the weight of evidence for evaluation of the category chemicals and should not be excluded from the overall data assessment.

Invertebrates. For the daphnia study, critical missing data elements are water temperature, DO, TOC, and test results corrected for 100 percent active ingredient For Mysidopsis bahia, missing data elements are pH, water temperature, DO, TOC, water hardness, and test results corrected for 100 percent active ingredient.

Temperature was included in the original robust summary. DO and TOC for daphnia and DO, TOC and water hardness for M. bahia were not reported. The revised Robust Summary (#18) included in the Supplement to Appendix A, attached, has been corrected to show that the calculated values are based on 100% active ingredient.

Some studies used in the Test Plan development, such as this assay, do not meet all current guideline requirements. The Task Group believes that these studies add to the weight of evidence for evaluation of the category chemicals and should not be excluded from the overall data assessment.

Algae. Missing data elements from robust summaries include pH, water temperature, DO, TOC, and water hardness. Also, for studies that had lower algal toxicity values, the submitter only provided limited information in a table in Appendix A. These data should be presented in a full robust summary format.

For the first reported study, the pH, hardness, alkalinity, and TOC have been added to the Robust Summary (#20) included in the Supplement to Appendix A, attached. Other data were not presented in the original studies. For the second series of studies summarized in the Robust Summary (#21), the starting pH and salinity of the cultures have been added and the Summary is included in the Supplement to Appendix A, attached. Other data were not provided in the original studies. Some studies used in the Test Plan development, such as this assay, do not meet all current guideline requirements. The Task Group believes that these studies add to the weight of evidence for evaluation of the category chemicals and should not be excluded from the overall data assessment.

CAS No. 61789-80-8

Fish. Several fish robust summaries were missing the following critical data elements: DO, water hardness, TOC, and test results corrected for 100 percent active ingredient.

For the first two reported studies, the temperature, dissolved oxygen and pH have been added to the Robust Summaries (#s 8-10) included in the Supplement to Appendix A, attached. Other data (TOC, hardness, alkalinity, etc.) were not available in the reports.

For the third Robust Summary, the data are included in a Robust Summary format because they help evaluate other reported values for the FND Cationic Category chemicals and the Task Group believes that they provide weight of evidence for the overall evaluation of aquatic toxicity.

Invertebrates. Key robust summaries need to be provided because only limited information was provided in a table format in Appendix A.

The data are included in a Robust Summary format because they help evaluate other reported values for the FND Cationic Category chemicals and provide weight of evidence for the overall evaluation of aquatic toxicity.

CAS No. 52467-63-7

Fish. Missing data elements are TOC and DO.

Dissolved oxygen has been added to the Robust Summary (#7) included in the Supplement to Appendix A, attached. TOC was not reported. Some studies used in the Test Plan development, such as this assay, do not meet all current guideline requirements. The Task Group believes that these studies add to the weight of evidence for evaluation of the category chemicals and should not be excluded from the overall data assessment.

Invertebrates. The missing data element is TOC.

The Robust Summary (#17) included in the Supplement to Appendix A, attached, has been updated to include water chemistry parameters summarized in the report (TOC was not reported). Some studies used in the Test Plan development, such as this assay, do not meet all current guideline requirements.

The Task Group believes that these studies add to the weight of evidence for evaluation of the category chemicals and should not be excluded from the overall data assessment.

Algae. Missing data elements are water hardness, DO, TOC, and test results corrected for 100 percent active ingredient.

The hardness, DO, and TOC are not reported. Some studies used in the Test Plan development, such as this assay, do not meet all current guideline requirements. The Task Group believes that these studies add to the weight of evidence for evaluation of the category chemicals and should not be excluded from the overall data assessment.

The Robust Summary (#19) included in the Supplement to Appendix A, attached, has been modified indicating that the values are based on 100% active ingredient.

CAS Nos. 68424-85-1 and 7173-51-5

The submitter should provide all applicable robust summaries for these analogs.

See previous response to availability of ADBAC and DDAC reports above (page 1).

Table 1: DDAC Report Submissions for Pesticide Reregistration
Pertinent to the HPV Chemical Challenge Program

DDAC Study	MRID Submission Number
Acute Toxicity to Fish (Bluegill)	MRID #41578001
Acute Toxicity to Fish (Coho)	MRID #41578003
Acute Toxicity to Aquatic Invertebrates (Daphnia)	MRID #41578002
Acute Toxicity to Aquatic Invertebrates (Mysid)	MRID #41578004
Acute Oral Toxicity (Rat)	MRID #42296101
13-week dermal toxicity study in rats	MRID #41305901
90-day feeding toxicity study in rats	MRID #40966302
52-week oral toxicity study in dogs	MRID #41970401
Chronic toxicity study in rats	MRID #41965101
Chronic toxicity study in mice	MRID #41802301
Bacterial mutagenicity	MRID #40282201
Chromosomal aberration	MRID #40705801
Unscheduled DNA synthesis	MRID #40895201
Two-generation reproduction (rat)	MRID #41804501
Developmental Toxicity (rat)	MRID #41886701
Developmental Toxicity (rabbit)	MRID #41018701